

## PREFACE

A final report is being submitted at this time for two reasons. First, a final report was requested by NASA Headquarters, Washington, D.C., and secondly, our continued support from NASA has been granted under a new grant number (NSG 9014, effective August 1, 1974). Therefore, the findings to date are being reported here as a final report relative to Grant NGR-19-011-008. Future findings will be reported as a Semi-Annual Status Report and a Final Technical Report as they pertain to Grant NSG 9014.

For convenience, this report consists of two parts. Part I discusses findings pertaining to Grant NGR-19-011-008, while Part II reports findings relative to Grant NGR-19-011-008 (Supplement #1).

(NASA-CR-140114) THE EFFECT OF  
CONTINUOUS LOW DOSE-RATE GAMMA IRRADIATION  
ON CELL POPULATION KINETICS OF LYMPHOID  
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## PART I

The Effect of Continuous Low Dose-Rate Gamma  
Irradiation on Cell Population Kinetics of Lymphoid Tissue\*

by

Bessie Ruth Foster\*\*

SCOPE, METHODS AND FINDINGS

The research involved a study of cellular response and cell population kinetics during lymphopoiesis in the thymus of the mouse under continuous gamma irradiation using autoradiographic techniques and specific labeling with tritiated thymidine (TdR-<sup>3</sup>H).

The problem studied was the mechanism of cell proliferation of lymphoid tissue of the mouse thymus under the stress of continuous irradiation at a dose rate of 10 roentgens (R) per day for 105 days (15 weeks). The aim was to determine whether or not a steady state or near-steady state of cell population could be established for this period of time, and what compensatory mechanisms of cell population were involved.

Exposure of the test animals to continuous irradiation was carried out at The Argonne National Laboratory. Subsequent studies on these subjects, which are briefly summarized below, have proceeded in what we describe as phases.

Unirradiated animals of the same age, strain, and sex were processed in a similar manner as irradiated mice. These mice served as controls.

Phase one of the study involved irradiation of one hundred, 29-day old BCF<sub>1</sub> male mice at a dose rate of 10R per day in order to obtain some information pertaining to changes in tissue weight. Four mice were removed from the irradiation unit, and sacrificed one hour following an intraperitoneal in-

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\*A research project that was jointly funded by NSF (Grant GB 29136) and NASA (Grant NGR-19-011-008) during the first two years of investigation. The research was initiated at the Argonne National Laboratory where the principal investigator was a participant in the Argonne Faculty Research Participation Program, summer, 1971. Research support during the final year of this study was sponsored by NASA (Grant NGR-19-011-008, Supplement #1).

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jection of TdR-<sup>3</sup>H at various time intervals up to 105 days. Standard techniques were employed to dissect lymphoid tissue, obtain tissue weights, cell counts, autoradiographs, etc.

#### Changes in Tissue Weight:

Changes in thymic tissue weight under continuous gamma irradiation at 10R per day were examined in 4-week old BCF<sub>1</sub> male mice at 0, 1, 2, 3, 4, 5, 6, 7, 10, 14, 18, 21, 24, 28, 35, 42, 49, 56, 63, 70, 77, 84, 91, 98, and 105 days. Figure 1 shows that initially there was an "out-burst" of growth seen by a sharp increase in tissue weight. This finding was interpreted as a "compensatory response" to the initial radiation stimulus. Thereafter, weights of irradiated thymuses seemed to parallel those of controls up to 49 days of irradiation at which time there was a significant increase in the weight of irradiated thymuses. A t-test on these data indicated that the difference was significant at the 5% level. A similar finding occurred at day 63 - however, in reverse order; that is, there was a significant decrease in the thymus weights among irradiated mice. This occurrence was followed by results that approximated each other in irradiated and control thymuses up to day 84. At this time there was a significant decrease in thymus weights among irradiated mice compared to controls up to day 98, with a steady state being achieved again by day 105, the termination day of radiation exposure for this study.

On the basis of thymus weights and tests of significance carried out on these data, it was concluded that the thymus in BCF<sub>1</sub> male mice seemed to maintain a steady or near-steady state of tissue growth up to 84 days of irradiation at a dose rate of 10R per day. At this time there was a "breakdown" in thymus tissue growth among irradiated mice for about two weeks with a steady state being achieved again by day 105 albeit at a much lower level than what appears to be normal.

#### Changes in Thymic Cell Counts:

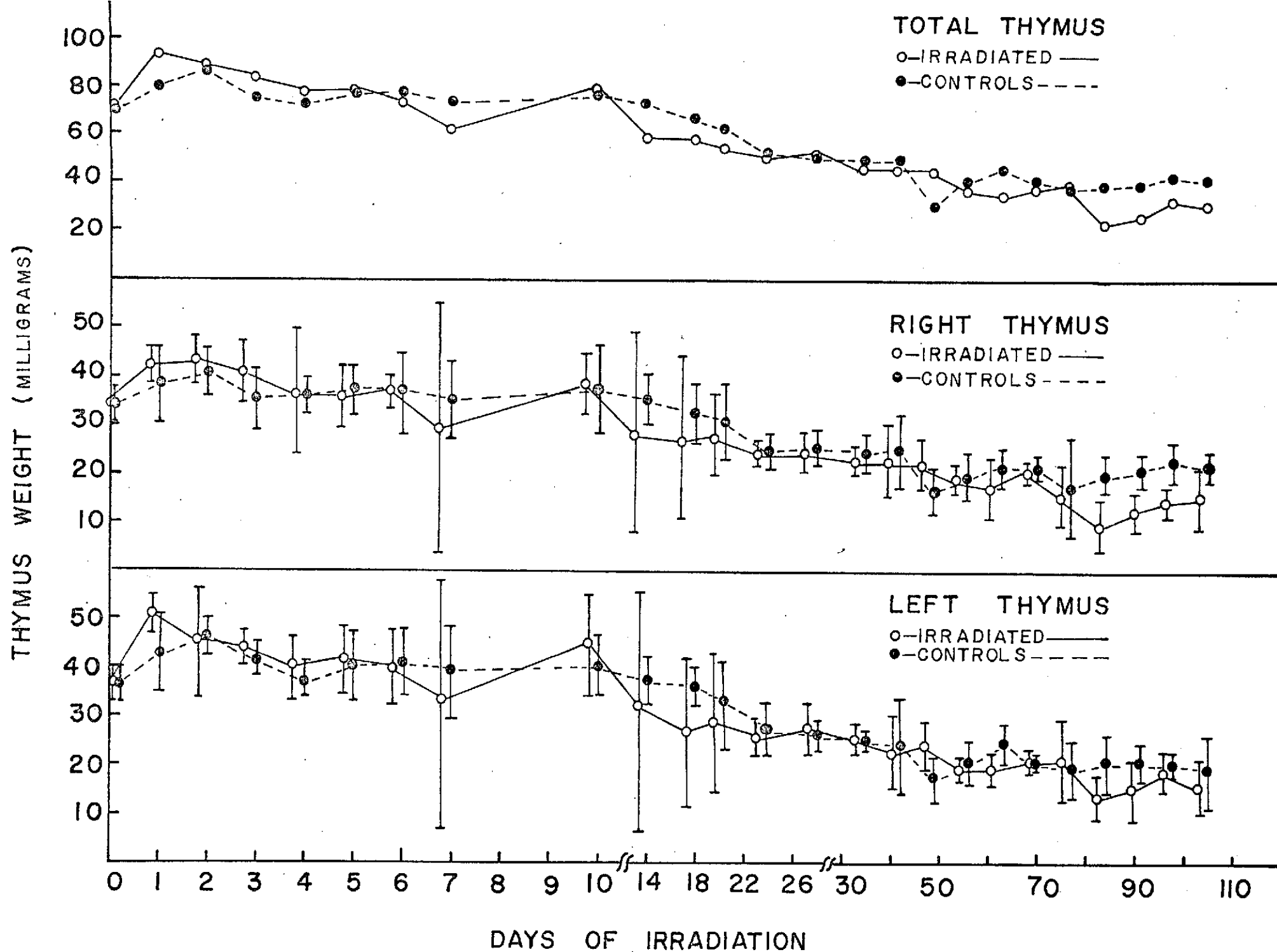


Figure 1

Thymic cell counts were examined in mice under continuous irradiation at the same dose rate and time intervals numerated previously. Unirradiated controls were processed similarly.

At the desired period of irradiation, 4 mice were removed from the irradiation unit, injected intraperitoneally with 1 microcurie of TdR-<sup>3</sup>H/gram body weight, sacrificed one hour after TdR-<sup>3</sup>H, and the appropriate tissue was dissected and processed for routine cell counting on a Coulter Counter. The cell counts were corrected for coincidence loss and background, and the results were plotted on graphs.

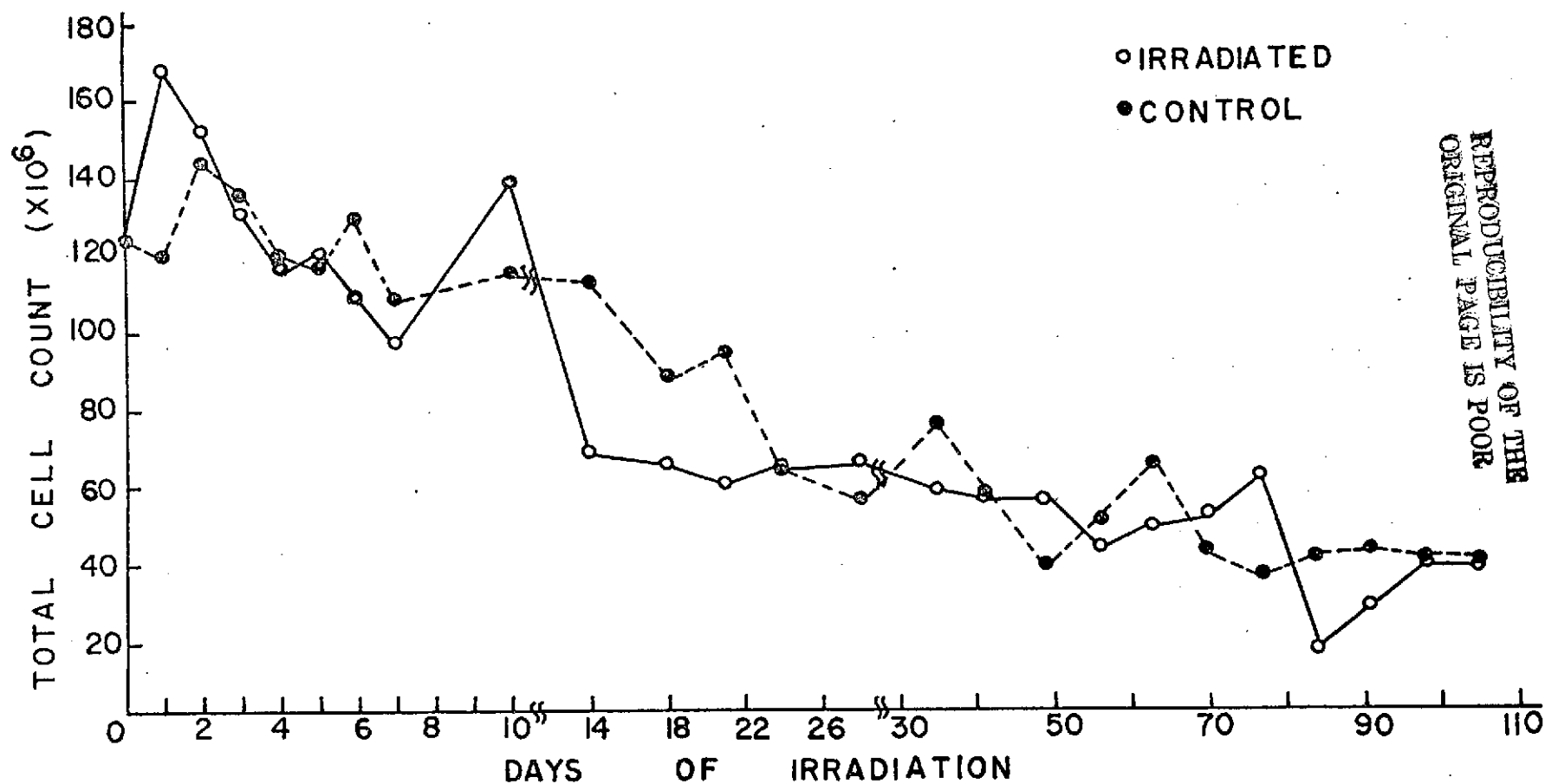
Figure 2 illustrates that at the onset of irradiation there was an "out-burst" of thymic cell production in the irradiated animals compared to that in similar controls. This finding was interpreted as an "over-production" of cells or "compensatory effect" in response to the initial radiation exposure.

As with the investigation on thymic weights, there seemed to have been a corresponding steady or near-steady state of proliferation, on the basis of cell counts, at about day 24 to day 84. After this time, the total cell count in thymuses of irradiated mice took on a lesser value than that in similar controls.

A t-Test on these data indicated that there was a significant difference in total cell counts at day 35, and at day 84-91 with what appeared to be normal levels reached again by day 98 throughout the remainder of the period of irradiation.

To determine whether or not thymic tissue was undergoing changes in "cellularity," that is, changes in the number of cells per unit mass of tissue, an analysis on the number of thymic cells/milligram of thymus was made. Figure 3 illustrates a graph of these data. Again, a steady or near-steady state of cellularity seemed to have been reached at about day 24. However, there was a marked increase in the number of cells/milligram of tissue in the irradiated thymuses at day 70 and day 77 compared to non-irradiated controls, with the

# RADIATION EFFECTS ON THYMIC CELL COUNTS



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Figure 2

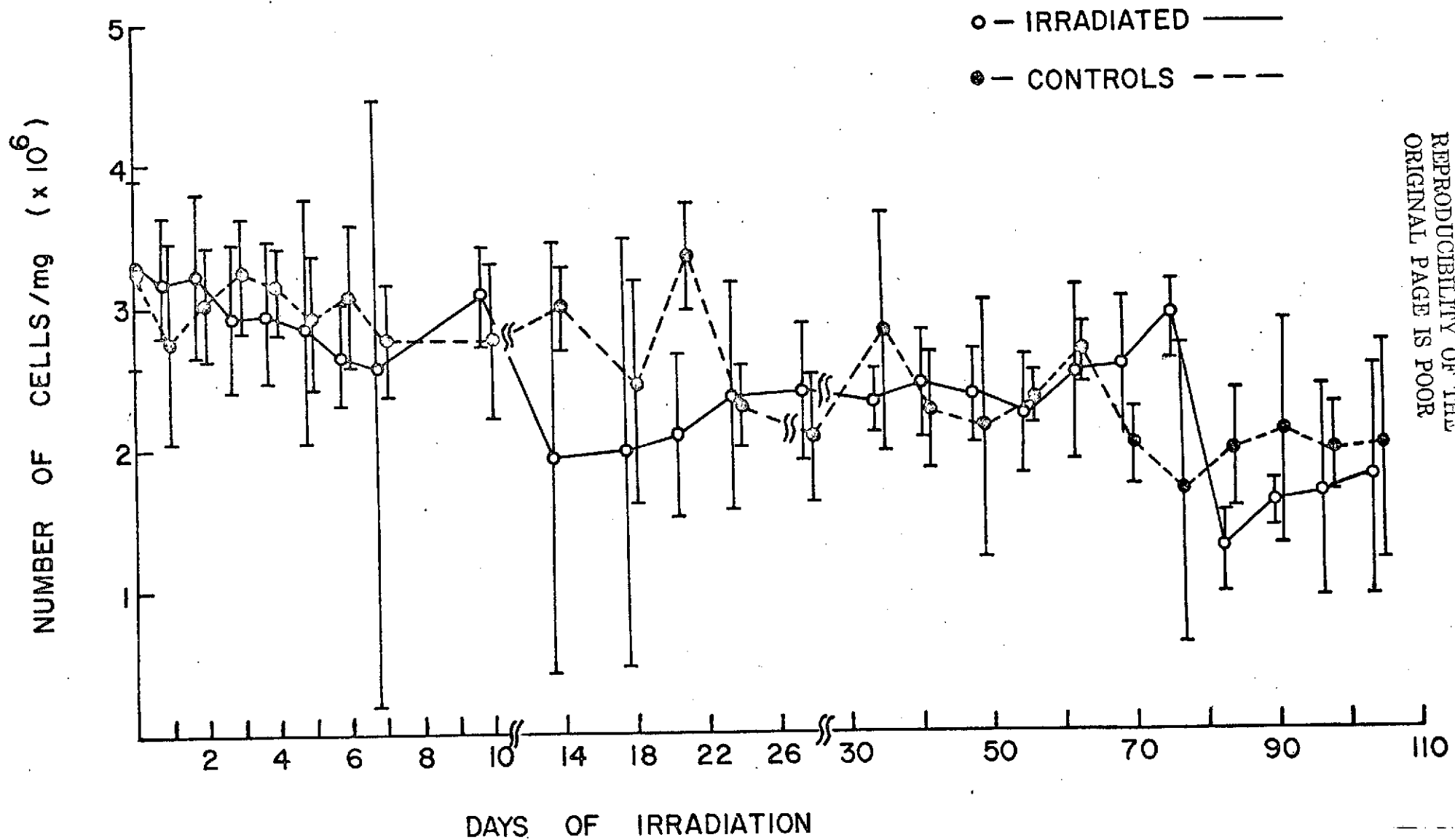


Figure 3



irradiated group taking on lesser values from day 84 through day 105.

A statistical analysis (t-Test) indicated that there was a significant difference in cells/milligram of thymus tissue at 24 days of irradiation and at day 77-84, with what appeared to be normal cellularity achieved again by day 91 and throughout the remainder of the irradiation period.

Findings discussed to this point suggested that on the basis of tissue weight and cell counts lymphoid tissue in BCF<sub>1</sub> male mice seemingly maintains a steady or near-steady state of cellular proliferation under continuous irradiation at a dose rate of 10R per day for about 84 days. At this time there is an apparent "breakdown" in tissue weights and cell counts for about 2 weeks with a near-steady state being achieved again by day 105.

The next phase of investigation was to examine the effect of continuous irradiation on the distribution of various lymphoid cell types and cell labeling in the thymus to ascertain some idea of the compensatory mechanisms involved in the steady or near-steady state phenomenon that is established.

#### Distribution of Thymic Cell Types and TdR-<sup>3</sup>H Labeling

Cell types considered here were of three classes: PAS-positive reticular cells, non-PAS-positive reticular cells and lymphocytes.

Right thymuses from mice irradiated for investigations discussed above were dissected, weighed to nearest milligram, fixed, sectioned, stained with perrodic acid-Schiff reagent, autoradiographed, counterstained with hematoxylin, examined microscopically, and the associated data were plotted graphically on Figure 4. This graph illustrates that initially, and throughout most of the period of investigation, there was generally a smaller percentage of PAS-positive cells in thymuses of irradiated mice compared to similar controls except from day 84 through day 105. At this time there was a sharp increase in the percentage of PAS-positive cells in irradiated thymuses. These differences were significant at the 5% level.

Since the presence of PAS-positive reticular cells suggests an increased

# RADIATION EFFECTS ON DISTRIBUTION OF PAS-POSITIVE CELLS IN THE THYMUS

○ IRRADIATED  
● CONTROL

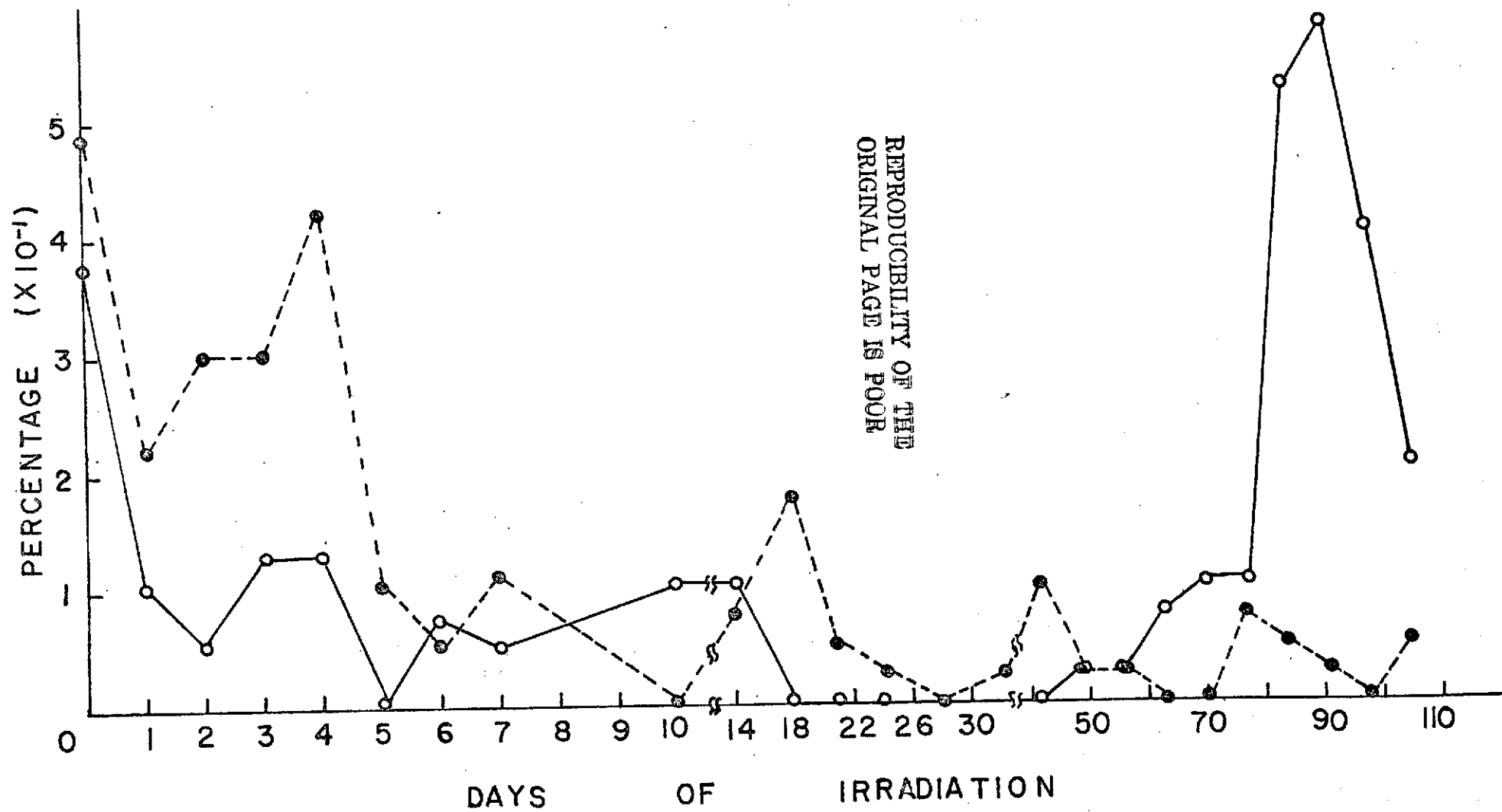


Figure 4

stimulus for mitotic activity, then one possible compensatory mechanism which re-establishes a near-steady state of cellular proliferation in the thymus by day 105 of irradiation seems to be an increased stimulus for cell division.

Regarding non-PAS-positive reticular cells, initially there was a smaller percentage of non-PAS-positive reticular cells in irradiated thymuses compared to similar controls for about 7 to 14 days of irradiation. After this, there was an increase in the percentage of non-PAS-positive reticular cells in irradiated thymuses from day 18 through day 70 followed by a decrease from day 77 throughout the remainder of the period of irradiation.

The percentage of lymphocytes ranged from 84 to 98 percent in both irradiated and control thymuses. Initially, there was a greater percentage of lymphocytes in irradiated thymuses compared to controls from about 7 to 14 days of irradiation. From day 18 through day 70 there was a smaller percentage of lymphocytes in irradiated thymuses followed by a greater percentage throughout the remainder of the irradiation procedure. In other words, from day 18 through day 70 there was a decrease in the percentage of lymphocytes in irradiated thymuses and a corresponding increase in non-PAS-positive reticular cells during this same period of time. Since reticular cells of the thymus are precursor cells which give rise to lymphocytes, these findings suggest that a second compensatory mechanism which serves to re-establish the near-steady state of cellular proliferation in the thymus under continuous irradiation is a state of "maturation arrest" among non-PAS-positive reticular cells. That is, a greater proportion of the thymus cell population remains in the "progenitor" or "precursor" state under continuous irradiation, thereby, producing cells which compensate for those that are damaged or destroyed by radiation.

Labeling indices were determined for the various cell types under con-

tinuous irradiation. Because of the very small number of PAS-positive cells present in both irradiated and control thymuses, labeling patterns were difficult to interpret. The labeling indices among PAS-positive cells in irradiated thymuses either paralleled or took on lesser values than those in controls except at about 70 days of irradiation at which time there was a sharp increase in labeling among PAS-positive cells compared to controls. It appears here that thymidine labeling among PAS-positive cells is not a contributing factor so far as maintaining the structural integrity of the thymus, but rather, the mere presence of the PAS-positive cell is what seems to stimulate mitotic activity.

Labeling patterns among non-PAS-positive reticular cells in irradiated thymuses were similar to those of controls with the irradiated group generally exhibiting a smaller labeling index.

Labeling among thymic lymphocytes is illustrated in Figure 5. This graph shows that there was less labeling in irradiated lymphocytes compared to controls for about 18 days. Thereafter, the labeling index among lymphocytes in irradiated thymuses was greater than that in controls. Since thymidine labeling suggests DNA synthesis which in turn suggests that cells are in preparation for division, a third compensatory mechanism which enables the thymus to maintain a near-steady state of cellular proliferation under continuous irradiation may be an increase in the "proportion of cells proliferating."

#### The Cell Cycle:

On the basis of thymus weights and thymic cell counts it was demonstrated that a seemingly steady state of cellular proliferation was achieved by about four weeks of continuous irradiation. In order to determine whether or not there were any changes in the generation time of thymic cells, a group of 40, four-week old BCF<sub>1</sub> male mice were exposed to continuous irradiation at a dose

# RADIATION EFFECTS ON LABELING IN THYMIC LYMPHOCYTES

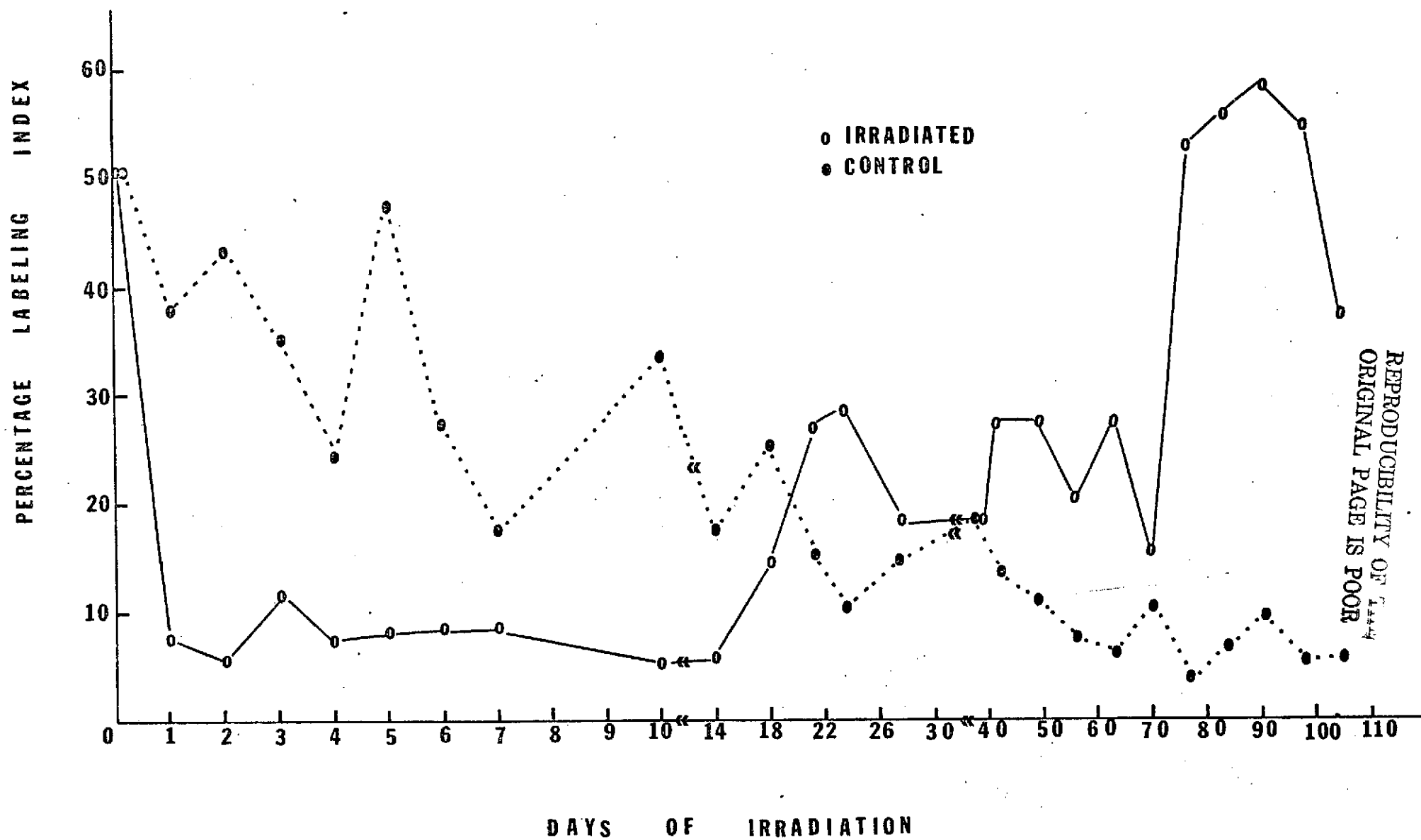


Figure 5

rate of 10R per day for 4 weeks, removed from the irradiation unit, injected intraperitoneally with TdR- $^3\text{H}$ , and sacrificed at various time intervals ranging from 0.5 to 30.0 hours following TdR- $^3\text{H}$ . Thymus tissue was dissected, fixed, processed through autoradiography, developed, stained, examined microscopically, and labeled mitoses scored at each sacrifice interval using routine histological and autoradiographic procedures.

Forty unirradiated mice of the same age, sex, and strain were processed similarly, these mice served as controls.

Two hundred mitotic figures were scored at each sacrifice interval, and data were graphed to form labeled mitosis curves as shown in Figure 6.

Although there was no well-defined descending limb of the first wave of mitosis nor was there a well defined second wave in irradiated nor in control thymuses, it was possible to roughly approximate a cell cycle time of about 10.5 hours in both groups. It was concluded, therefore, that changes in the cell cycle time in thymuses irradiated at 10 R per day were not contributing compensatory mechanisms.

Since there was no apparent change in the generation time of thymus cells in irradiated mice compared to controls, the next line of investigation was to determine the distribution of lymphocyte classes, thymidine labeling, proliferative fraction, and relative proliferative capacity among each lymphocyte class in order to determine which cell type(s) was contributing most to the proliferative activity of the cell system.

#### Distribution of Lymphocyte Classes and TdR- $^3\text{H}$ Labeling:

One hundred, 29-day old BCF<sub>1</sub> male mice were irradiated at a dose rate of 10 R per day for 105 days. Four mice were removed from the irradiation unit and sacrificed one hour following an intraperitoneal injection of TdR- $^3\text{H}$  at various time intervals until 105 days had elapsed. Standard techniques

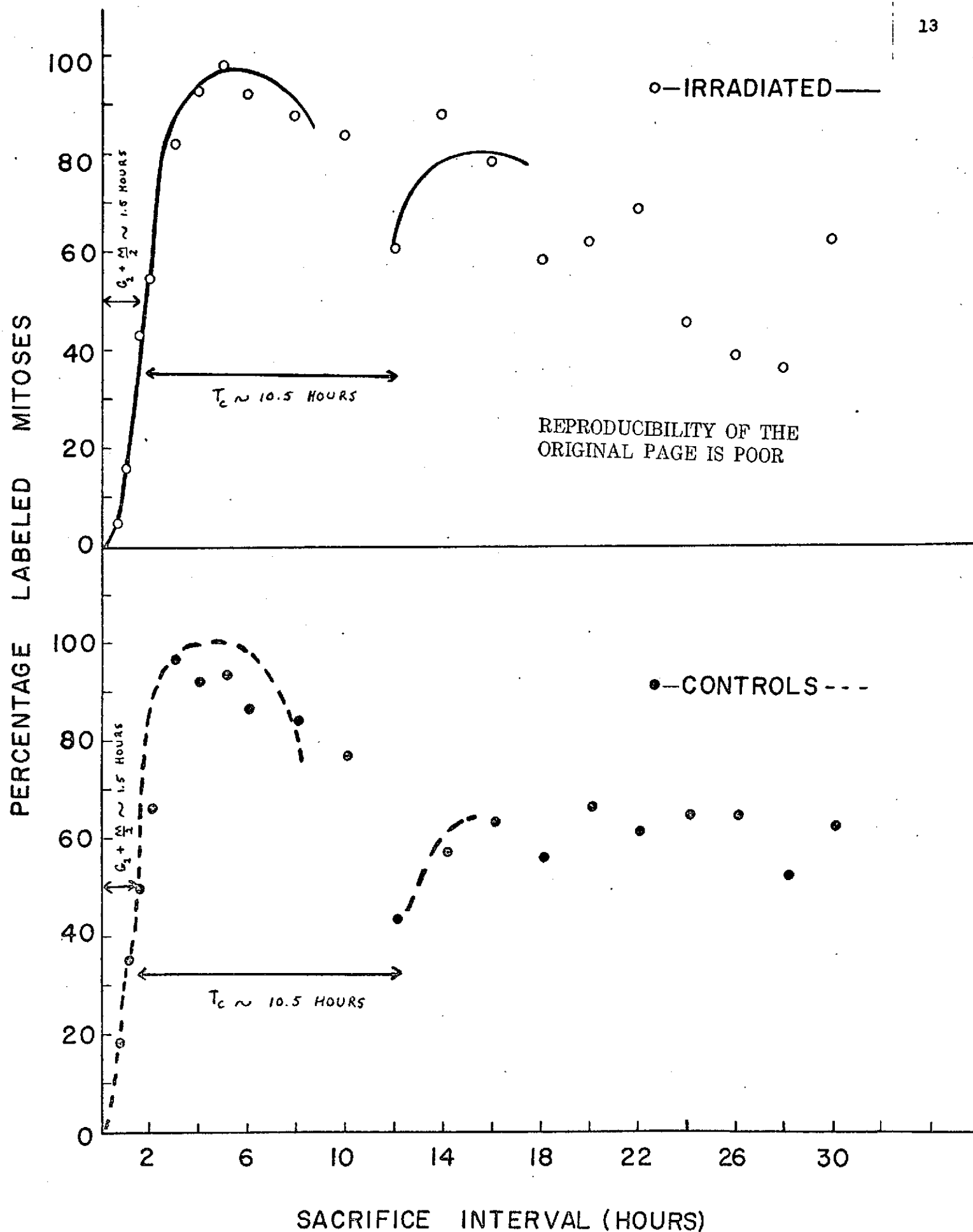


Figure 6

were used to process the tissue through autoradiography with subsequent staining and microscopic examination.

One hundred unirradiated mice of the same strain, sex, and age as the irradiated group were processed in a similar manner. These mice served as controls.

Cells were classified on the basis of morphology and size as reticular cells, large, medium, and small lymphocytes.

For convenience and because of their relative numbers, data on medium and small lymphocytes were sometimes pooled.

Data on the distribution of reticular cells (Figure 7) and various lymphocyte classes indicated that there was generally an increase in the proportion of reticular cells among irradiated thymuses compared to controls. Since lymphopoiesis in the thymus appears to occur as a result of a-symmetric division of reticular cells into lymphocytes of progressively decreasing sizes, an additional compensatory mechanism under continuous irradiation seems to be an increase in the proportion of precursor cells.

There was generally a smaller proportion of large lymphocytes among irradiated thymus tissue compared to controls, with a very few exceptions.

Data on medium and small lymphocytes were pooled (Figure 8). These data illustrated that there was a very slight increase in the proportion of medium and small lymphocytes among irradiated thymuses compared to controls throughout most of the irradiation period. Because of the relative numbers of medium and small lymphocytes, and since the small lymphocyte is generally thought to be non-dividing in vivo, this finding suggested that the medium lymphocyte was contributing an appreciable amount to the proliferative activity of the cell system.

Thymidine labeling among reticular cells and various lymphocyte classes



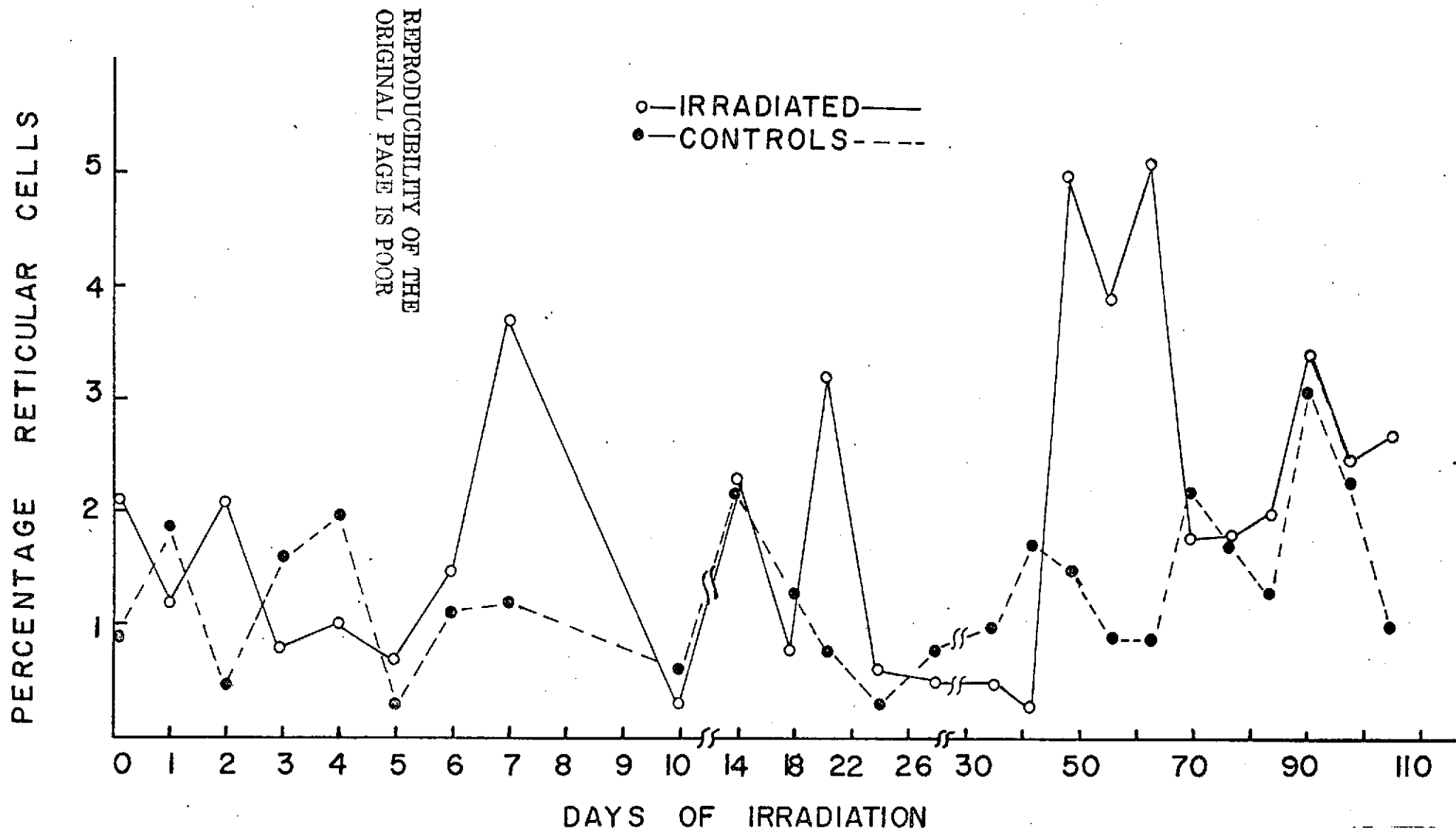


Figure 7

PERCENTAGE MEDIUM & SMALL LYMPHOCYTES

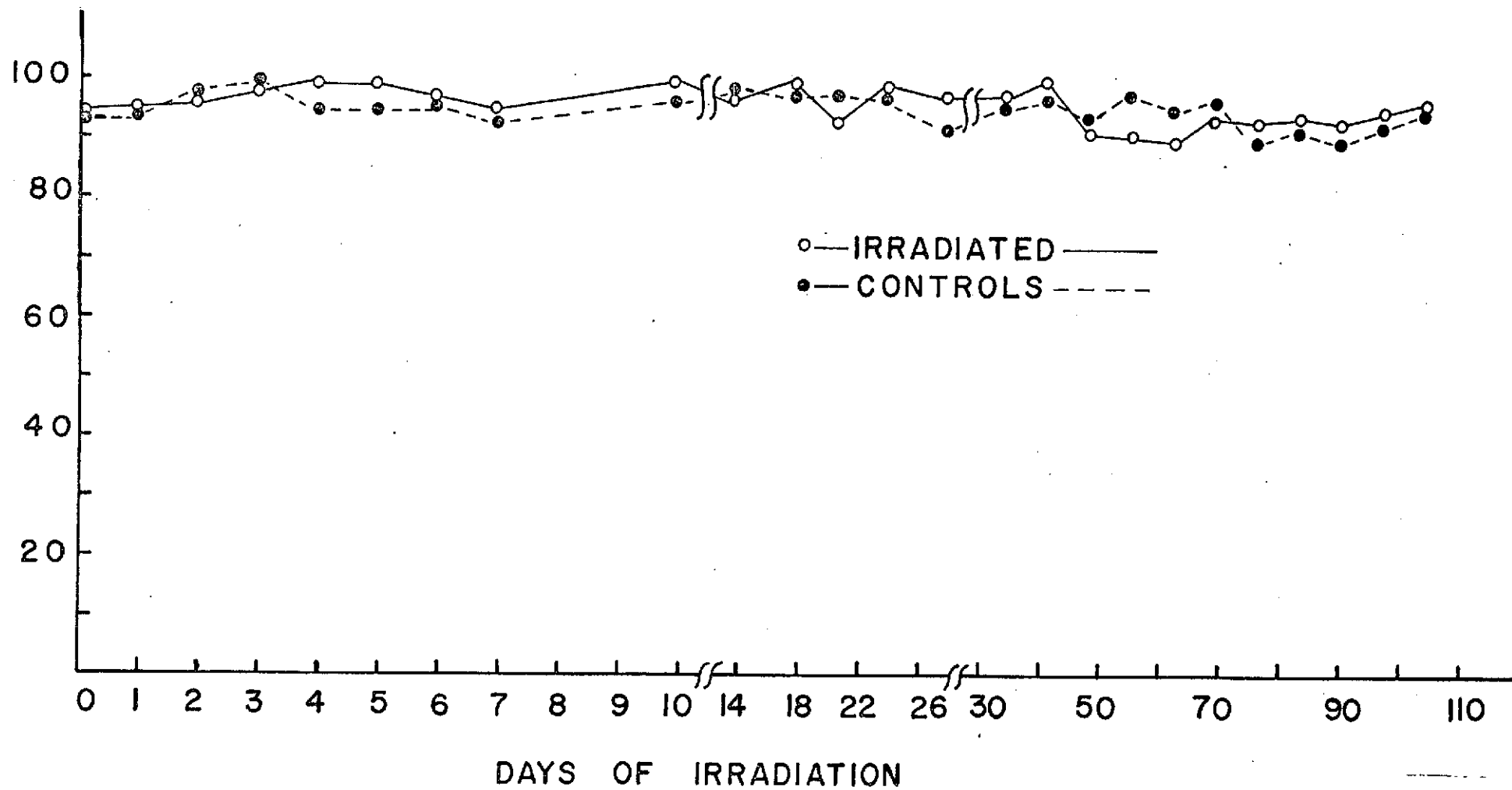


Figure 8

was examined. There was generally less labeling in irradiated reticular cells and among large lymphocytes compared to controls. However, among the medium and small lymphocyte category there was an increase in labeling in irradiated groups during the initial and final phase of the irradiation period.

The relative increase in labeling among the medium and small lymphocyte category further suggests that the medium lymphocyte, in particular, is contributing appreciably to the proliferative activity of the thymus cell population.

The final phase of investigation pertaining to Part I of the research was to determine the proliferative fraction and the relative proliferative capacity (RPC) among reticular cells and among the various classes of lymphocytes. That is to say, what proportion of a given cell population is in preparation for division, meaning the cell will perhaps divide, and what is the relative proliferative capacity which means how effective a cell class is in its capacity to proliferate compared to other cell classes.

#### The Proliferative Fraction and Relative Proliferative Capacity:

The proliferative fraction of reticular cells and of different lymphocyte classes was examined. Figure 9 illustrates that only in the medium and small lymphocyte categories was there an appreciable increase in the proliferative fraction during the initial and final phase of the irradiation period. These findings further suggested that it was the medium lymphocyte category that contributed most to the proliferative activity of the thymus.

Because of the volume of data accumulated an average was taken over the entire period of irradiation for each cell type, and these data are reported here. On an average there was about 85% of the reticular cell population proliferating, 75% of the large lymphocytes, 20% of the medium lymphocytes and about 5% of the small lymphocytes.

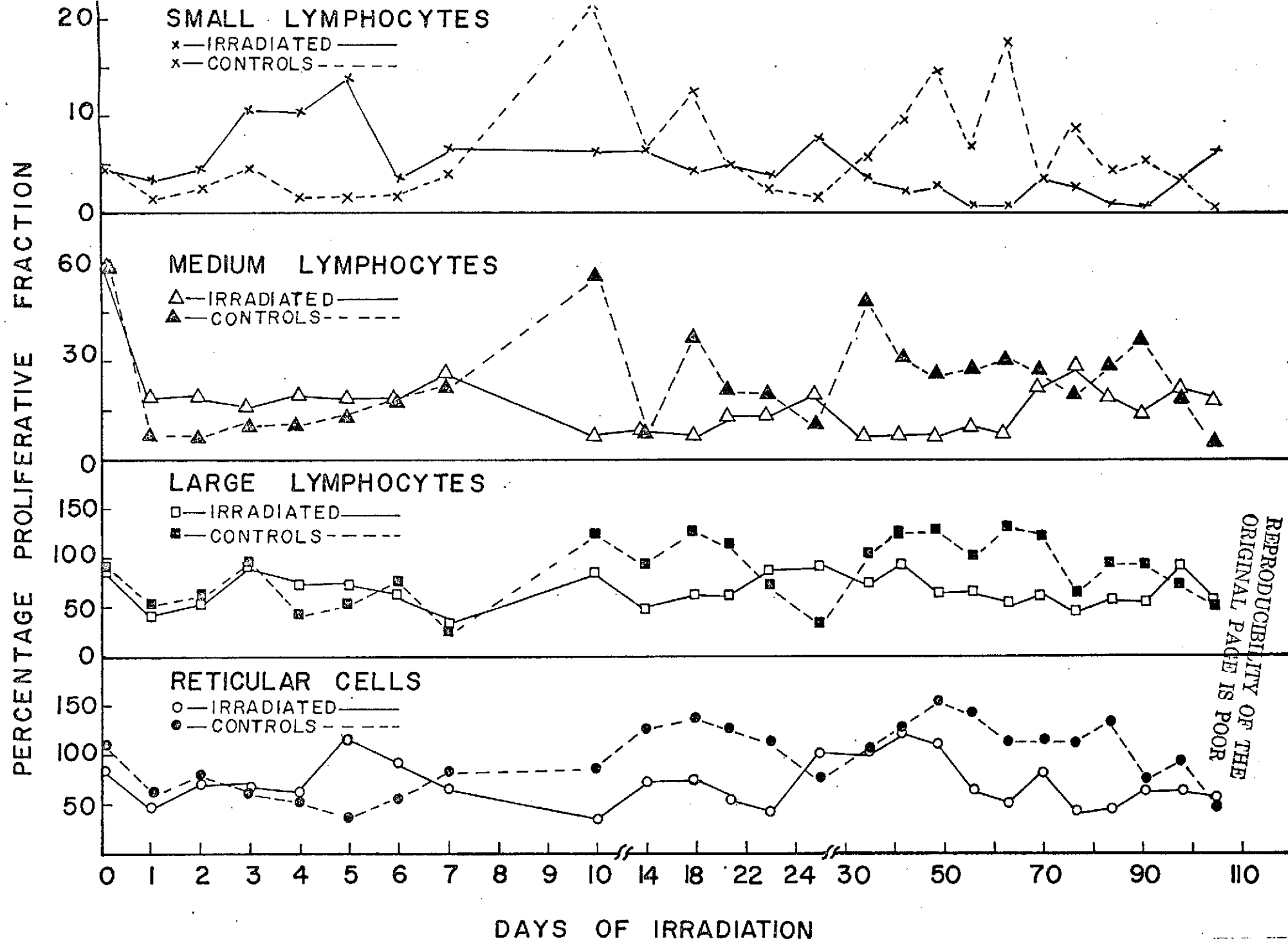


Figure 9

Regarding the relative proliferative capacity among thymic cell types (Figure 10), there was generally an increase in the RPC among irradiated reticular cells compared to controls throughout most of the irradiation period. Also, there was an increase in the RPC among medium and small lymphocytes during the initial and final phases of the irradiation period. Most importantly, the medium lymphocyte exhibited an RPC of about 4 times that of reticular cells, and about 2 times that of large and small lymphocytes.

#### Summary and Conclusions

On the basis of tissue weights, cell counts, distribution of PAS-positive cells, labeled mitoses, distribution of lymphocyte classes, proliferative fractions, and relative proliferative capacities of thymus cells under continuous irradiation, it was concluded that the response of this cell system to a radiation dose of 10 R per day for 105 days is seemingly bi-phasic. That is, the first steady state phenomenon is reached by about 24 days of irradiation to about day 84. At this time, there is a significant decrease in tissue weight, cell counts, etc., for about 2 weeks which is interpreted as a "breakdown" in the system. By day 98 through the remainder of the irradiation period (day 105), another steady state of cellular proliferation obtains.

Since there are two populations of lymphocytes -"short-lived" and "long-lived", it may be that the first steady state phenomenon is governed by the short-lived lymphocytes, and the second steady state phenomenon might possibly be mediated by long-lived lymphocytes.

The duration of the second steady state phenomenon is beyond the scope of this study inasmuch as our irradiation period terminated after 105 days. More extensive research needs to be done to assess the duration of the second steady state of cellular proliferation in the mouse thymus under continuous irradiation at a dose rate of 10 R per day.

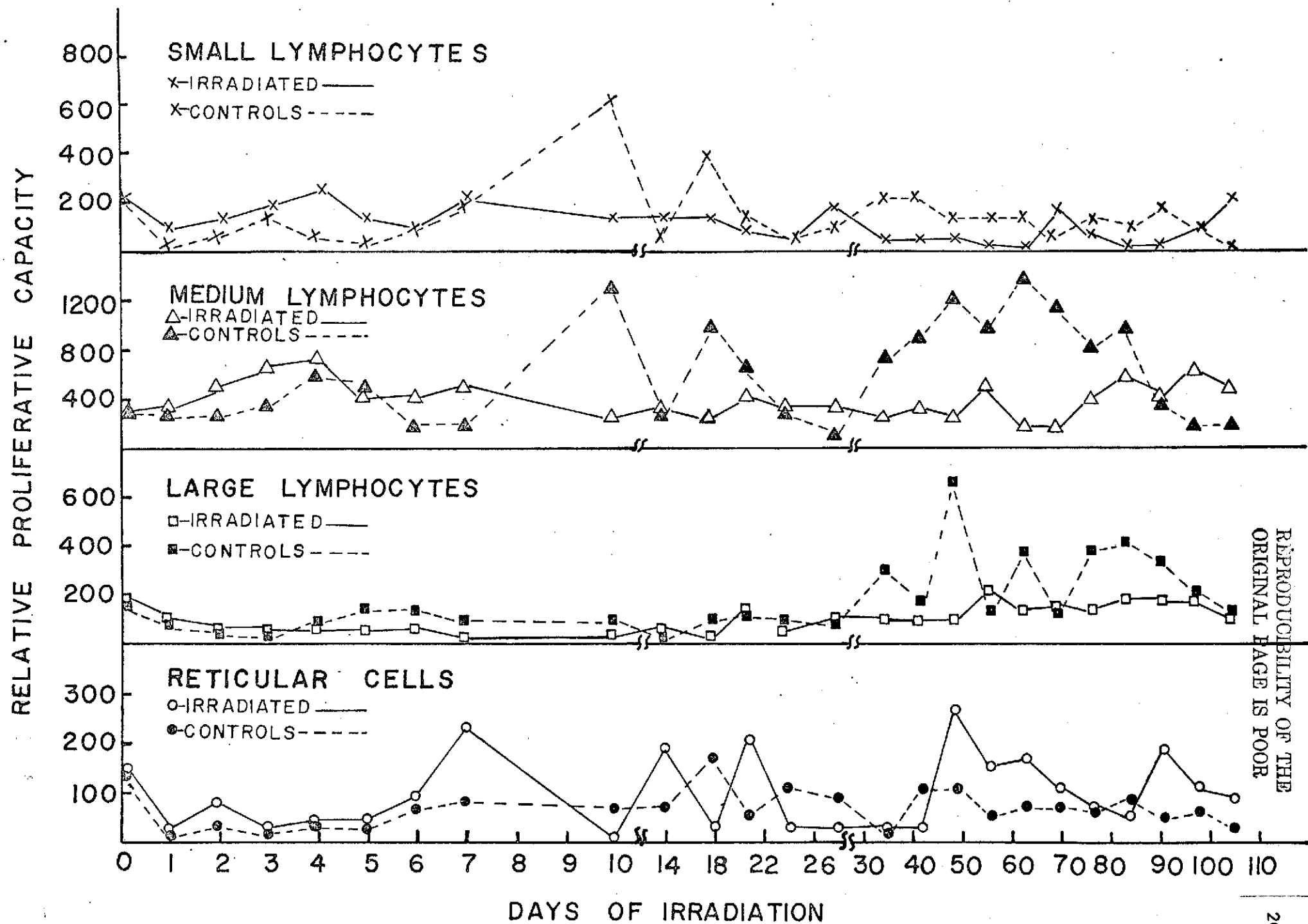


Figure 10

Compensatory mechanisms which enabled the radiation-depleted cell population to achieve a steady state were:

- (1) an increase in the proportion of PAS-positive cells
- (2) maturation arrest of precursor cells
- (3) increase in the proportion of cells proliferating, and
- (4) an increase in the proportion of precursor cells.

Lastly, it was the medium lymphocyte which contributed most to the proliferative activity of the thymus cell population.

PART II



Lymphoid Cell Kinetics Under Continuous Low Dose-Rate  
Gamma Irradiation - A Comparison Study\*

SCOPE, METHODS AND FINDINGS

Part II of the research involved making a comparison study of the effect of continuous low dose-rate gamma irradiation on cell population kinetics of lymphoid tissue of the mouse spleen (white pulp) with findings as they relate to the mouse thymus.

On the basis of thymidine labeling and distribution of various cell types in the thymus under continuous irradiation, it was concluded and reported in Part I that at least four compensatory mechanisms served to maintain a near-steady state of cellular proliferation:

- (1) an increase in the proportion of PAS-positive cells
- (2) maturation arrest of precursor cells
- (3) increase in the proportion of cells proliferating, and
- (4) an increase in the proportion of precursor cells.

It was the purpose of Part II of this study to determine whether or not the spleen responds to continuous irradiation in a similar fashion as the thymus.

All findings reported here were obtained on two hundred mice (100 irradiated and 100 controls). Four mice were removed from the irradiation unit and sacrificed one hour following an intraperitoneal injection of TdR-<sup>3</sup>H at various time intervals up to 105 days. Standard techniques were employed to dissect lymphoid tissue, obtain tissue weights, autoradiographs, etc. Mice which served as controls were of the same age, sex and strain as those treated with irradiation. Data points on figures and those in tables included in this report represent an average taken on 4 animals.

Changes in Tissue Weight:

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\*Research sponsored by NASA (Grant NGR-19-011-008, Supplement #1)

Figure 11 illustrates weight changes that occurred in spleen during the irradiation period. As in the thymus, the spleen also exhibited an "outburst" of growth after the initial radiation treatment. Following this, there was a significant difference among weights in irradiated spleens versus controls for about 18 days of irradiation with higher weight values shifting from controls to irradiated and back to controls. By day 21, the spleen had achieved a steady-state of growth, for there was no significant difference among tissue weights in the two groups. However, the steady state phenomenon was very short-lived, lasting for only a few days. At day 24 through day 42 there was a significant decrease in weights among irradiated spleens, followed by another short-lived period of steady-state growth for about a week encompassing day 49. From day 56 through day 98 there was another decrease in tissue weights among irradiated spleens. A t-Test on these data indicated that these differences were significant at the 5% level. By day 105, irradiated spleens had again achieved a steady state of tissue growth.

#### Changes in Tissue Weight/Gram Body Weight

Weight changes in thymus and spleen tissue per gram body weight were examined under continuous irradiation at various time intervals from day zero to day 105. Figure 12 along with Tables 1 and 2 illustrate changes that occurred. As reported previously, there was an "outburst" of cellular proliferation in irradiated tissue at the onset of irradiation in both the thymus and the spleen. This finding is interpreted as a "compensatory response" to the initial radiation treatment. Thereafter, the weights in control and irradiated thymuses/gram body weight paralleled each other throughout the remainder of the 105 day irradiation period. However, this was not the case with the spleen. From about day 35 through day 91, there was a marked decrease in the weight of the spleen per gram body weight in irradiated animals. These

# RADIATION EFFECTS ON SPLEEN WEIGHT

○ IRRADIATED

● CONTROL

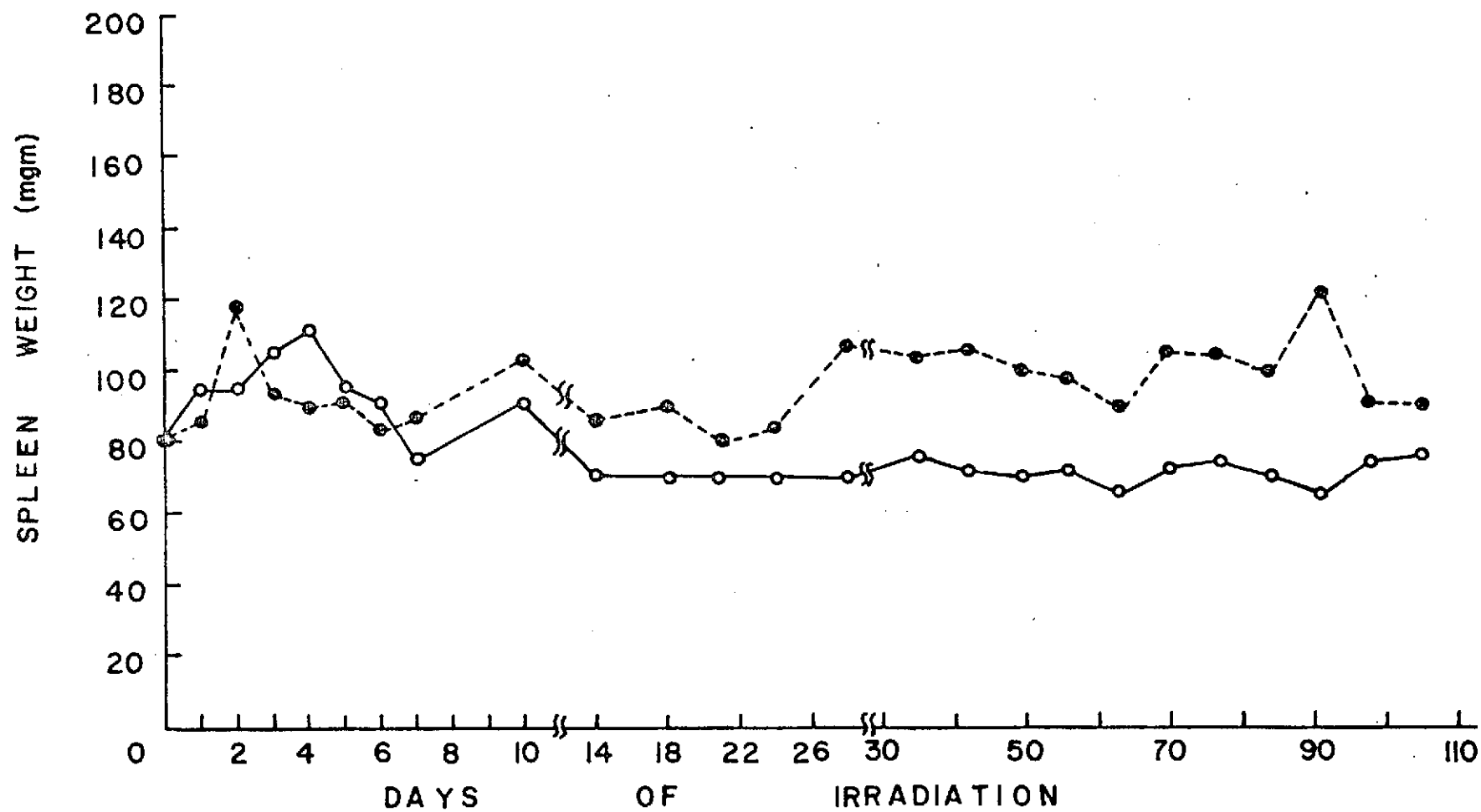


Figure 11

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# RADIATION EFFECT ON LYMPHOID TISSUE WEIGHT

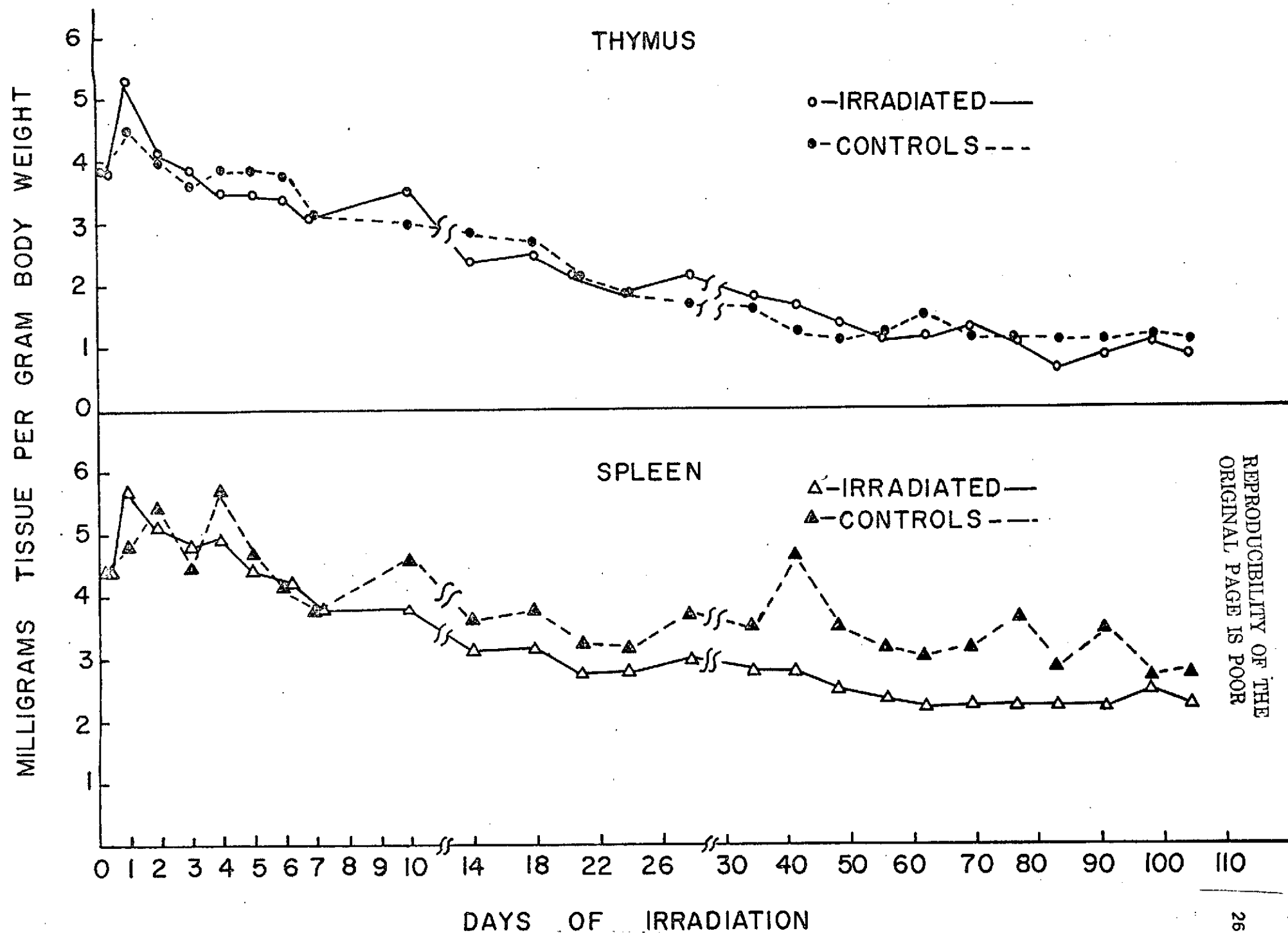


Figure 12

findings are consistent with findings of other investigators. Neary, Munson and Mole (1957) observed that under continuous gamma irradiation, the weights of the mouse thymus and spleen were:

TABLE 1

## Thymus Weights Under Continuous Irradiation

Days of Irradiation	Thymus Weights, Controls (mg)	Thymus Weights, Irradiated (mg)	Milligrams Thymus/ Gram Body Weight, Controls (mg/g)	Milligrams Thymus/ Gram Body Weight, Irradiated (mg/g)
0	71.2	71.2	3.9	3.9
1	80.7	92.8	4.5	5.4
2	87.2	88.5	4.0	4.2
3	76.5	83.8	3.7	3.9
4	73.0	76.8	3.9	3.5
5	76.7	76.0	3.9	3.5
6	77.7	75.5	3.8	3.4
7	74.0	61.5	3.3	3.1
10	68.7	82.2	3.0	3.5
14	71.7	56.3	2.9	2.4
18	67.2	56.5	2.7	2.5
21	63.5	55.3	2.6	2.2
24	51.5	50.0	1.9	2.0
28	5.2	51.3	1.8	2.2
35	49.2	47.0	1.7	1.8
42	41.0	44.0	1.3	1.7
49	33.0	44.5	1.2	1.4
56	39.7	36.8	1.3	1.2
63	44.7	35.3	1.5	1.2
70	41.0	39.8	1.2	1.3
77	36.5	36.0	1.3	1.1
84	38.0	22.3	1.1	0.7
91	39.5	27.3	1.1	0.9
98	42.0	32.3	1.2	1.1
105	39.5	30.0	1.1	0.9

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TABLE 2

Spleen Weights Under Continuous Irradiation				
Days of Irradiation	Spleen Weights, Controls (mg)	Spleen Weights, Irradiated (mg)	Milligrams Spleen/ Gram Body Weight, Controls (mg/g)	Milligrams Spleen/ Gram Body Weight, Irradiated (mg/g)
0	82.2	82.2	4.5	4.5
1	87.0	97.5	4.9	5.7
2	119.7	97.5	5.5	4.6
3	94.5	107.2	4.6	4.9
4	90.2	112.7	4.8	5.1
5	93.2	97.0	4.7	4.5
6	84.7	95.2	4.1	4.2
7	88.7	76.8	3.9	3.9
10	104.2	93.0	4.6	3.9
14	87.0	72.0	3.6	3.1
18	91.7	71.5	3.7	3.2
21	81.5	70.5	3.4	2.8
24	84.5	71.0	3.2	2.8
28	108.2	71.5	3.7	3.0
35	104.2	77.5	3.5	2.9
42	140.7	73.2	4.6	2.8
49	100.0	81.0	3.5	2.5
56	99.2	92.8	3.2	2.4
63	91.0	69.8	3.3	2.3
70	107.0	73.0	3.2	2.3
77	105.2	74.5	3.6	2.3
84	100.5	71.5	2.9	2.3
91	122.0	65.8	3.5	2.3
98	91.5	70.2	2.7	2.5
105	90.2	76.8	2.6	2.3

maintained at a dose rate of 16 R per day for 15 weeks, the spleen being affected more. At 40 rads per day, Lamerton, Pontifex, Blackett and Adams (1960) and Lamerton (1966) observed that peripheral blood lymphocyte counts in rats fell by 20 days, then rose, and recovery with normal spleen weight was maintained with animals surviving up to 30 weeks. In splenectomized rats, the rise after 20 days was not seen, and blood lymphocyte levels stabilized at a lower level than normal. Brecher, Brambel and Brambel (1964), observed low peripheral blood lymphocyte counts, collapse of splenic lymphoid follicles, and marked splenic erythropoiesis in rats after 70 rads per day for 12 weeks.

It is of interest to note that even though the radiation dose rate which we employed was very low (10 R/day), we observed similar weight changes in the thymus and spleen that other investigators observed at higher dose rates. Thus, lymphatic tissue is among the most radiosensitive tissue of the body as reported by Trowell (1952, 1961) and Vos (1967).

#### Summary and Conclusions

On the basis of tissue weights, it can be concluded that the response of both the thymus and spleen to continuous low dose-rate irradiation is multiphasic. That is, alternating periods of steady-state growth, followed by "collapse," which in turn is followed by another period of homeostasis. Since there are two populations of lymphocytes - "short-lived" and "long-lived," it may be that different phases of steady-state growth are mediated by different lymphocytes. Possibly, the first steady state of growth is governed by short-lived lymphocytes, while the second steady state may be governed by long-lived lymphocytes.

Although there is a multiphasic response of both thymus and spleen tissue to continuous low dose-rate irradiation, with both tissues achieving a steady state of growth by day 105, the spleen is affected to a greater extent with shorter periods of steady-state growth than exhibited by the thymus.

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#### PUBLICATIONS, THESES, INVENTIONS AND DISCOVERIES, AND SCIENTIFIC COLLABORATORS

##### Publications

The following publications have been made pertaining to the research, copies of which have been forwarded to NASA Scientific and Technical Information Facility.

- (1) Foster, B.R. The Effect of Continuous Low Dose-Rate Gamma Irradiation on Tissue and Body Growth. The Louisiana Physics Teacher. Volume 3, Number One, Spring 1973, pp. 17-19.
- (2) Foster, B.R., Taylor, B., LeFear, P. and Ware, M. Biphasic Response of Lymphoid Tissue Under Continuous Irradiation. Radiation Research. Volume 59, Number 1, July 1974, p. 304 (Abstract).

At least one other publication will be made in the form of a research paper in Radiation Research, the manuscript of which is in preparation.

##### Theses

No thesis was prepared in connection with the research.

##### Inventions or Discoveries

No inventions nor discoveries were made in connection with the research.

##### Scientific Collaborators

The scientific collaborators connected with the grants include one senior scientist, and a total of 20 pre-baccalaureate students who studied and worked with the project at some given time. The senior scientist is Dr. R.J.M. Fry of The Argonne National Laboratory, Argonne, Illinois, who served as my advisor during the summer, 1971, when I was a participant in the Argonne Faculty Research Participation Program. During this time (summer, 1971), the initial phase of the study, that is, the irradiation of the test animals, was carried



out in the laboratory of Dr. Fry.

The following pre-baccalaureate students studied and worked with the project:

Billy Taylor - physics major (graduated)  
 Joseph Alexander - physics major (senior)  
 Joseph Blow - mathematics major (graduated)  
 Neda Bailey - mathematics major (senior)  
 Ronnie Blake - chemistry major (senior)  
 William Wiley, III - physics major (junior)  
 Alan Kennedy - chemistry-computer science major (junior)  
 Matthew Ware - physics major (senior)  
 Caffin Gordon - sociology major (graduated)  
 Dorothy Baker - business major (graduated)  
 Sharon Harris - pre-medicine major (junior)  
 Patricia LeFear - physics major (junior)  
 Don Blow - mathematics major (senior)  
 Cynthia Tizeno - physics major (sophomore)  
 Michael Banks - political science major (sophomore)  
 Larry Nicks - chemistry major (sophomore)  
 Gerry Mansfield - physics major (freshman)  
 Dennis Dowell - physics major (freshman)  
 Angelia Young - biology major (unclassified)  
 Gregory Route - recreation major (graduated)

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#### COMMENTS

##### General

Other than making possible the development of a well-equipped research laboratory and the research project per se, the greatest contribution that the research grants made to the University was the involvement of undergraduate students in research procedures. Students became familiar with routine laboratory and research procedures, learned how to manipulate research equipment, and became adept in collecting and interpreting data. Research experiences which the students realized will be beneficial to them in graduate school, industry, or whatever career they choose to pursue.

The funds allocated for student support enabled some students to earn their college tuition or other fees, many of whom would not have been able to pursue a college career otherwise. I personally hope that NASA will continue to look favorably upon research proposals that actively involve undergraduate students

at developing institutions.

Comments on Continuation

NASA has granted us renewed support for one year under a new grant number (NSG 9014), effective as of August 1, 1974. Any findings obtained under the new grant will be reported as a semi-annual or final report with said grant number.